DETAILED ACTION

In view of the appeal brief filed on 1/7/2008, PROSECUTION IS HEREBY REOPENED. New grounds of rejection set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

Claims 1 and 3-4 are pending.

Claims 3-4 are withdrawn from consideration.

Claim 1 is under consideration.

All the rejections stated in the final office action dated 8/29/2006 are withdrawn in view of new ground(s) rejection in this office action. Applicant's arguments in the Appeal Brief for the rejections based on the references in combination with respect to claim above have been considered but are moot in view of the new ground(s) of rejection below.

Claim Objections

Claim 1 is objected to because of the following informalities: the claim recites LAK activity, which is defined in the specification (page 1) and the record of the art as Lymphokine-Activated Killer Cell activity. However, in order to avoid the confusion of LAK activity with the other activity, such as the

enzyme activity, the abbreviation LAK should be spelled out when first used in the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tani et al., (anticancer Res, page 1773-1776, 1993, provided in the office action, 12/20/2005) in view of Yamamoto et al., (Biosci Biotechnol Biochem, Vol 61, p 1909-12, 1999, provided in the office action 4/6/2005), Liu et al., (Immunopharmacology, vol 40, page 187-198, published 11/23/1998, provided in the office action, 12/20/2005), Mizoguchi et al., (Gastroenterol Jpn. Vol 22: page 459-464, 1987, provided in the office action, 5/04/2007) and Nagaoka H. (US Patent No. 6090615, filed Dec. 1996).

The claim is drawn to a method for determining whether an extract of Lentinus edodes mycelium has a Lymphocyte activated killing (LAK) activity-enhancing effect suitable for a subject comprising the step of isolating lymphocyte fraction, treating the lymphocyte with extract of Lentinus edodes mycelium, measuring/comparing the activity of the LAK activity, wherein the extract of Lentinus edodes mycelium is prepared by a method comprising the step of crushing the lentinus edodes mycelium in the presence of water and additive enzymes (cellulose, protease, or glucosidase) and raise the temperature to inactivate the enzymes.

Lymphocyte activated killing (LAK) is defined as Lymphokine (IL-2) Activated Killer (NK) cells as evidenced by Mesh Word Search (see attached).

Tani et al., teach a method of augmentation of LAK activity by Lentinan (LNT), the active components from the extract of *Lentinus edodes mycelium* (LEM, page 1773, col 1, line 9+). Tani et al., teach method steps comprising isolated peripheral blood cells and preparing IL-2 activated NK lymphocytes, measuring and comparing the enhanced LAK activity of NK cells treated with LNT of LEM (figure 2, page 1774). Tani et al., teach that the LAK activity stimulated by IL-2 is enhanced by LNT from the LEM (entire article).

Tani et al., do not teach that the LAK activity is enhanced by the extract of LEM and do not teach how to prepare the extract of LEM or LNT of LEM including in the presence of one or more enzymes (cellulose, protease, or glucosidase) and raising the temperature of said suspension to inactivate the enzymes.

Yamamoto et al., teach a method of determining the cytotoxicity of lymphocytes, specifically NK cells, induced by a fraction (JLS-18) of extract of Lentinus edodes mycelium (LEM, page 1910-1911, and figure 1). Yamamoto et al., teach method steps, preparing NK lymphocytes, and measuring and comparing the LAK activity of NK cell treated with the fraction of LEM (page 1909-10, section materials and result).

Liu et al., further define the mechanism of the argumentation of (enhancing) LAK activity of NK cells by the extract of LEM. Liu et al., first teach that the LNT enhances the LAK activity (page 188, col 1) and increases the production of IL-2 in the mononuclear cells comprising T- and NK lymphocytes treated with the extract (page 188, section 2.1 and page 193-4, figure 4-5). Liu et al., then teach that the activity of enhancing of LAK is due to the production of Lymphokines, such as IL-2, induced by the extract of LEM (page 187, abbreviation, line 6 and page 188, col 1, line 3). Liu et al., also teach a method of preparing the LNT and the extract from LEM comprising extraction with boiling water at 90-100 ºC, which indicates that LNT is stable in heat condition and further characterize the component of Lentinan (LNT) as polysaccharide-peptide complex (page 188, section 2.1). As stated above, LAK activity is IL-2 activated NK cell activity, which would be enhanced by increasing the amount of IL-2 produced by lymphocytes or NK cells treated with the extract of LEM or LNT.

Mizoguchi et al., teach a detailed method of preparing the extract of LEM having anti-tumor and virus activity by enhancing the immunoresponse (entire article). The method steps comprising that LEM are crushed and delignified in a solid medium composed of sugar-can bagasse and defatted rice bran, digested with mycelia enzymes, and finally extract of LEM were heated to 60 ºC that would inactivate some of the enzymes (page 461). The contents of mycelia enzymes although are not specified by Mizoguchi et al in the article, they could contain one or more enzymes including cellulas, protease and/or glucosidase that digest cellulose, protein, and/or sugar of the LEM.

Nagaoka H. teach a method of preparing an extract of LEM, which has antitumor or virus activity (col 1, line 30+) by adding one or more of enzymes of cellulose, protease, and/or glucosidase and then heating the extract up to 95 ºC to inactivate the enzyme (col 1, line 60+, col 3 and col 6-9).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the methods for determining the LAK activity of the extract of LEM with expected result. One of ordinary skill in the art at the time the invention was made would have been motivated to combine and apply the method of making the exact of LEM by Nagaoka H. and Mizoguchi et al., and Liu et al., to the method of Tina et al., and/or Yamamoto et al., in order to determine the effect of enzyme-digested extract of LEM on the LAK activity for the benefit of or more efficiently treating a tumor or infection because Liu et al and Tani et al, teach and suggest the enhancing LAK activity by a component of LEM extract, LNT. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success to make the extract of LEM by adding additional enzymes to digest the celluloses, proteins and/or sugars in the LEM and then to inactivate the enzymes at high temperature because inactivation of the digested enzyme is necessary step known by one skilled in the art and because both Nagaoka et al and Liu et al have shown increasing temperature in the preparation the extract of LEM do not destroy the activity of the extract. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the teachings to determine the enhancing LAK activity by the extract of LEM because Tani et al., have shown the method steps for enhancing the LAK activity by the major component, LNT, Yamamoto et al., have shown the method and steps of determining LAK activity by fraction of LEM extract and Liu et al further showed the

mechanism of enhancing the LAK by the extract of *LEM*. To combine all the teachings together, one skilled in the art would arrive the claimed invention and therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

In addition, since the claim does not define what the active component in the extract of LEM for the LAK activity is, the prior art LNT from the extract of LEM taught by Tani et al., appears to meet the requirements of the instant claims. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao, Ph.D./
Examiner, Art Unit 1642

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643